AMENDMENTS TO THE SPECIFICATION

Please replace the Specification as filed with the Substitute Specification submitted herewith. The Substitute Specification only contains subject matter from the original Specification and previously entered amendments under 37 C.F.R. 1.121.

Please amend the Substitute Specification as follows:

Please replace paragraph [0006] with the following paragraph:

The lack of sensitivity of the method is illustrated by the fact that it cannot detect directly amplicons resulting from genetic amplification (PCR). A double amplification with primer(s) bearing a T3 or T7 sequences and then a ~~retrotranscription~~ **reverse transcription** with ~~a~~ **an** RNA polymerase. These RNA are cut into pieces of about 40 bases before being detected on an array (example 1 of WO 97/29212). However, long DNA or RNA fragments hybridize very slowly on capture probes present on a surface. Said methods are therefore not suited for the detection of homologous sequences since the homology varies along the sequences and so part of the pieces could hybridize on the same capture probes. Therefore, a software for the interpretation of the results should be incorporated in the method for allowing interpretation of the obtained data.

Please replace paragraph [0013] with the following paragraph:

A further aim of the invention is to provide such method and device which are based upon a simplified technology requiring the use **of a** single primer(s) in an amplification step and which allow the identification (detection and/or quantification) of a specific target sequence by the identification and/or recording of a single spot signal upon said microarray, said signal resulting only from the specific binding of the target sequence with its corresponding capture sequence.

Please replace paragraph [0016] with the following paragraph:

Figure 3 presents the effect of the length of the ~~specific~~ **spacer** sequence of a capture nucleotide sequence on the discrimination between sequences with different level of homology.

Please replace paragraph [0027] with the following paragraph:

The method according to the invention can be performed by using a specific identification (diagnostic and/or quantification) kit or device comprising at least an insoluble solid support upon which are bound ~~single-stranded~~ **single-stranded** capture nucleotide

sequences (preferably bound to the surface of the solid support by a direct covalent link or by the intermediate of a spacer) according to an array with a density of at least 4, preferably at least 10, 16, 20, 50, 100, 1000, 4000, 10 000 or more, different ~~single-stranded~~ **single-stranded** capture nucleotide sequences/cm^2 insoluble solid support surface, said ~~single-stranded~~ **single-stranded** capture nucleotide sequences having advantageously a length comprised between about 30 and about 600 bases (including the spacer) and containing a sequence of about 10 to about 60 bases, said sequence being specific for the target (which means that said bases of said sequence are able to form a binding with their complementary bases upon the sequence of the target by complementary hybridisation). Preferably, said hybridisation is obtained under stringent conditions (under conditions well-known to the person skilled in the art).

Please replace paragraph [0028] with the following paragraph:

In the method and kit or device according to the invention, the capture nucleotide sequence is a sequence having between 16 and 600 bases, preferably between 30 and 300 bases, more preferably between 40 and 150 bases and the spacer is a chemical chain of at least ~~6,8~~ **6.8** nm long (of at least 4 carbon chains), a nucleotide sequence of more than 30 bases or is nucleotide derivative such as PMA.

Please replace paragraph [0032] with the following paragraph:

If the homology between the sequences to be detected is low (between 30 and 60%), parts of the sequence which are specific in each sequence can be used for the design of specific capture nucleotide sequences binding each of the different target sequences. However, it is more difficult to find part of the sequence sufficiently conserved as to design "consensus" sequences which will amplify or copy all desired sequences. If one pair of consensus primers is not enough to amplify all the homologous sequences, then a mixture of two or more primers pairs is added in order to obtain the desired amplifications. The minimum homologous sequences amplified by the same consensus primer is two, ~~nut~~ **but** there is no limitation to said number.

Please replace paragraph [0040] with the following paragraph:

The method according to the invention can be performed even when a ~~target present between an~~ homology (or sequence identity) **between a target present and other molecules is** greater than 30%, greater than 60% and even greater than 80%~~ and other molecules~~.

Please replace paragraph [0043] with the following paragraph:

Another important aspect of this invention is to use ~~very concentrate~~ **a high concentration of** capture nucleotide sequences on the surface. If **the concentration is** too low, the yield of the binding is ~~quickly~~ **much** lower and is undetectable. Concentrations of capture nucleotide sequences between about 600 and about 3,000 nM in the spotting solutions are preferred. However, concentrations as low as about 100 nM still give positive results in favourable cases (when the yield of covalent fixation is high or when the target to be detected is ~~single stranded~~ **single-stranded** and present in high concentrations). Such low spotting concentrations would give density of capture nucleotide sequence as low as 20 fmoles per cm^2. On the other side, higher density was only limited in the assays by the concentrations of the capture solutions, but concentrations still higher than 3,000 nM give good results.

Please replace paragraph [0044] with the following paragraph:

The use of these very high concentrations and long probes are two unexpected characteristic features of the invention. The theory of DNA hybridisation proposed that the rate of hybridisation between two DNA complementary sequences in solution is proportional to the square root of the DNA length, the smaller one being the ~~limited~~ **limiting** factor (Wetmur, J.G. and Davidson, N. 1968, J. Mol. Biol. 3, 584). In order to obtain the required specificity, the specific sequences of the capture nucleotide sequences had to be small compared to the target. Moreover, the targets were obtained after PCR amplification and were ~~double stranded~~ **double-stranded** so that they reassociate in solution much faster than to hybridise on small sequences fixed on a solid support where diffusion is low thus reducing even more the rate of reaction. It was unexpected to observe a so large increase in the yield of hybridisation with the same short specific sequence.

Please replace paragraph [0045] with the following paragraph:

The amount of a target which "binds" on the spots is very small compared to the amount of capture nucleotide sequences present. So there is a large excess of capture nucleotide sequence and there was no reason to obtain the binding ~~if~~ **with** even more capture nucleotide sequences.

Please replace paragraph [0050] with the following paragraph:

Another application is the detection of homologous genes from a consensus protein of the same species, such as various cytochromes P450 by specific capture nucleotide sequences with or without the presence of a consensus capture nucleotide sequence for all the cytochromes possibly present in a biological sample. Such detection is performed at the gene level by ~~retrotranscription~~ **reverse transcription** into cDNA.

Please replace paragraph [0053] with the following paragraph:

Advantageously, the target to be identified is labelled ~~previously~~ **prior** to its hybridisation ~~with~~ **to** the single-stranded capture nucleotide sequences. Said labelling (with known techniques from the person skilled in the art) is preferably also obtained upon the amplified sequence ~~previously~~ **prior** to the denaturation (if the method includes an amplification step).

Please replace paragraph [0055] with the following paragraph:

Detection of genes is also a preferred application of this invention. The detection of homologous genes is obtained by first ~~retrotranscription~~ **reverse transcription** of the mRNA and then amplification by consensus primers as described in this invention.

Please replace paragraph [0056] with the following paragraph:

According to a further aspect of the present invention, the method, kit (device) or apparatus according to the invention is advantageously used for the identification of different *Staphylococcus* species or variant**s**, preferably the *S. aureus*, the *S. epidermidis*, the *S. saprophyticus*, the *S. hominis* or the *S. haemolyticus* for homologous ~~organs~~ **organisms** present together or separately in the biological sample, said identification being obtained by detecting the genetic variants of the *FemA* gene in said different species, preferably by using a common ~~locations~~ **location** in the *FemA* genetic sequence.

Please replace paragraph [0058] with the following paragraph:

The detection of the 12 MAGE according to the invention is presented in ~~figure 4 and 5 and~~ in example ~~4~~ **9**. The array allows to read the MAGE number by observation of the lines positive for signal bearing the specific capture probes ~~(example 5)~~.

Please replace paragraph [0059] with the following paragraph:

The same application was developed for the Receptors Coupled to the G Proteins (RCGP). These receptors bind all sort of ligands and are responsible for the signal transduction to the cytoplasm and very often to the nucleus by modulating the activity of the transcriptional factors. Consensus primers are formed for the various subtypes of RCGP for dopamine and for serotonine and histamine (~~figures 6 and 7 and example 4~~ **examples 10-12**). The same is possible for the histamine and other ligands.

Please replace paragraph [0060] with the following paragraph:

The detection of the various HLA types is also one of the applications of the invention (~~figure 7 and~~ example **13**). HLA are homologous sequences which differ from one individual to the other. The determination of the HLA type is especially useful in tissue transplantation in order to determine the degree of compatibility between the donor and the recipient. It is also a useful parameter for immunisation. Given the large number of subtypes and the close relation between the homologous sequences it was not always possible to perfectly discriminate one sequence among all the other ones and for some of them there was one or two cross-reactions. In these cases, another capture probe was added on the array which gives a reaction with the sequence to be detected and another cross-reaction, in order to make the identification absolute.

Please replace paragraph [0061] with the following paragraph:

There are several forms of Cytochrome P450 which are also homologous sequences. ~~Figure 9~~ **Example 14** presents the design of the array to identify several cytochromes P450 after ~~retrotranscription~~ **reverse transcription** and amplification with consensus primers ~~(example 6)~~.

Please replace paragraph [0069] with the following paragraph:

Advantageously the standard is added ~~in~~ **to** the initial biological sample or after the extraction step and is amplified or copied with the same primers and/or has a length and a GC content identical or differing ~~from~~ **by** no more than 20% ~~to~~ **from** the target. More preferably, the standard can be designed as a competitive internal standard having the characteristics of the internal standard found in the document WO98/11253. Said internal standard has a part of its sequence common to the target and a specific part which is different. It also has at or near its two ends sequences which are complementary of the two primers used for amplification or copy of

the target and similar GC content (WO98/11253). In the preferred embodiment of this invention, the common part of the standard and the target, means a nucleotide sequence which is homologous to all target amplified by the same primers (i.e. which belong to the same family or organisms to be quantified).

Please replace the header on page 16 immediately before paragraph [0075] with the following header:

Example 1: Detection of homologous *FemA* sequences on array bearing long specific capture nucleotide sequences ~~(Fig. 3)~~

Please replace paragraph [0088] with the following paragraph:

The target amplicons were 489 bp long while the capture nucleotide sequences were 47, 67 or 87 bases ~~single stranded~~ **single-stranded** DNA with a specific sequence of 27 bases **(Fig. 3)**.

Please replace the header on page 21 immediately before paragraph [0093] with the following header:

Example 5: effect of the length of the specific sequence of the capture nucleotide sequence on the discrimination between homologous sequences ~~(figure 3).~~